Molecular Design of C-Pivot Tripodal Ligands: Importance of the Glycerol Structure for Effective Complexation toward Alkali Metal Cations

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A new series of C-pivot tripodal ligands **1**−**4** containing a 2-methylglycerol unit were prepared and their complexation properties toward alkali metal cations were examined by measuring the extractability, stability constant in THF, characteristic absorption in the UV spectrum, change in the chemical shift in the ^{1}H NMR, and competitive passive transport. This type of compound (**1**−**4**) was found to possess excellent complexing ability and higher selectivity than another type of tripodal ligand **5** derived from tris(hydroxymethyl)ethane. This remarkable difference in the stability constants was reasonably explained by considering that the former takes a three-dimensional coordination toward alkali metal cations by cooperatively using the three electron-donating arms but the latter does not. This finding clearly shows that a proper selection of the structure of the basic skeleton is important for the molecular design of C-pivot tripodal ligands.

Introduction

Increasing attention has been focused on molecular recognition for specific guest molecules.[1,2] A number of cyclic and noncyclic host compounds have been developed and successfully modified with respect to the structures of the guest molecules. High complexing ability and selectivity have been realized by the recent progress in the molecular design of macrocyclic host compounds such as crown ethers, cryptands, spherands, and calixarenes, while the structures of the host compounds have become increasingly complicated. On the other hand, in connection with the properties of natural acyclic ionophores such as nigericin and monensin, a variety of noncyclic multidentate ligands for alkali metal cations have also been developed.[3−5] Generally speaking, acyclic host compounds have an advantage in their simple synthetic routes, but their complexing ability and selectivity are often poor because of their conformational freedom. Among noncyclic synthetic ionophores, however, Vögtle *et al*. reported excellent complexing abilities for N-pivot tripodal ligands containing a triethanolamine skeleton.[6] This excellent complexing ability for alkali metal cations should be ascribed to a three-dimensional coordination by the three electron-donating arms of the ligand. Although the change of the pivot atom from nitrogen to carbon is expected to remarkably affect their complexation properties as observed in the study of lariat ethers,[7] attempts at such change have rarely been made.[8] From this standpoint, we will describe the design and synthesis of C-pivot tripodal ligands and their complexation properties toward alkali metal cations.[9]

Results and Discussion

Design and Synthesis of Ionophores. To attain high complexing ability for alkali metal cations in C-pivot tripodal ligands, the three electron-donating arms must be arranged to cooperatively work for the uptake of the cation. Therefore, it is important to properly select a basic skeleton containing the pivot carbon. Previously, in the study on C-pivot lariat ethers,[8] we found that the methyl group at the pivot carbon plays an important role in the coordination of the electron-donating sidearm to the alkali metal cation captured by the crown ring. On the basis of this finding, we designed compounds **1**−**4** containing a 2-methylglycerol moiety, and the oxyquinoline unit was selected as the terminal coordination group of noncyclic multidentate ligands because of its excellent coordination property (Chart 1).[3,4] Compound **5** having a tris(hydroxymethyl)ethane skeleton was prepared as the reference to verify the effect of the connecting moiety.

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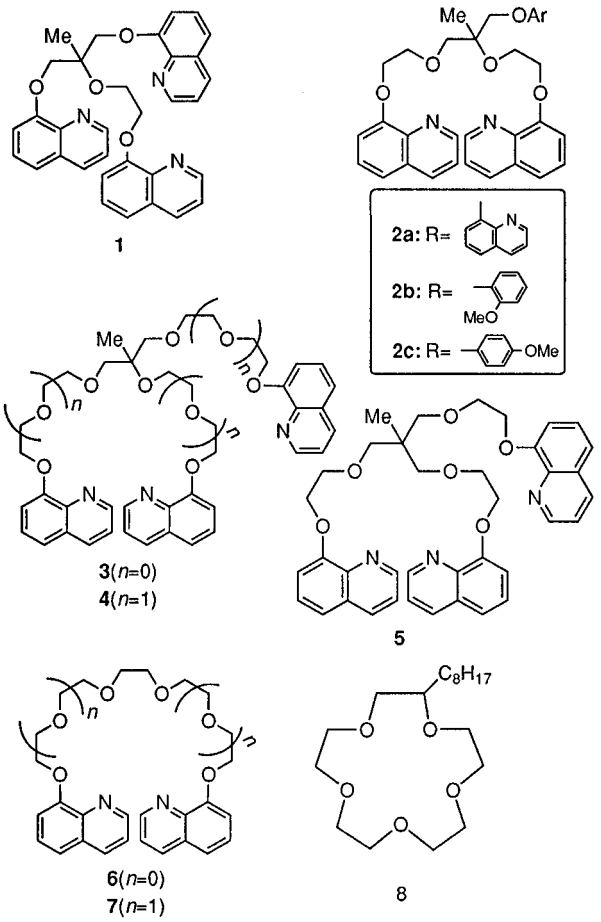
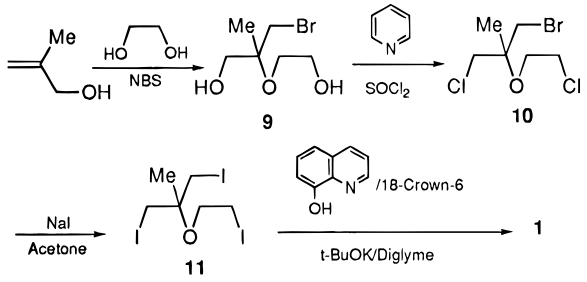
Chart 1

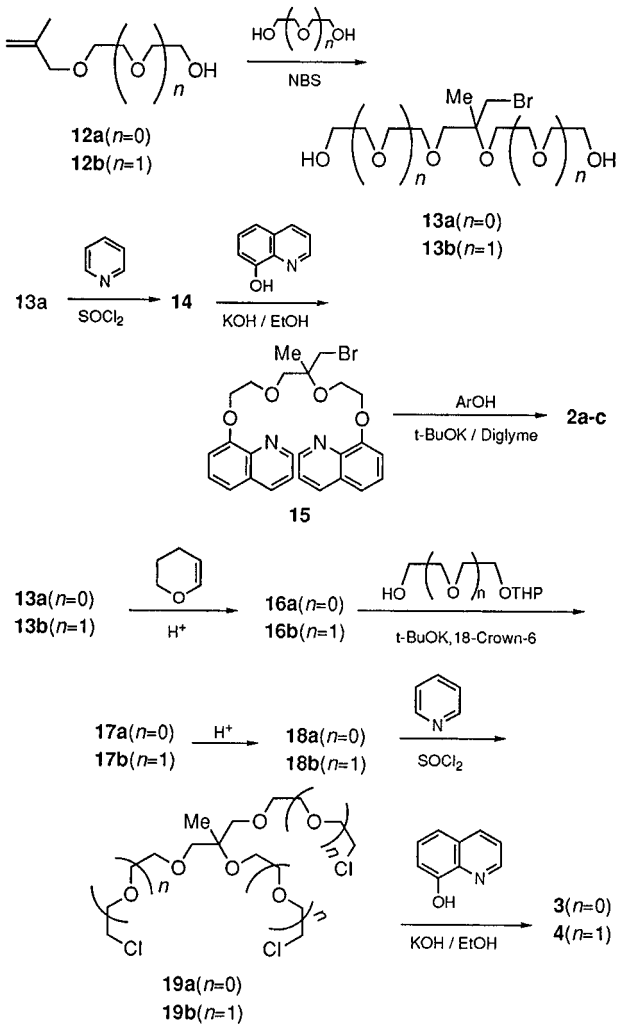


Scheme 1



The synthetic procedure of ligand **1** is shown in Scheme 1. *β*-Methallyl alcohol was bromoalkoxylated with *N*-bromosuccinimide (NBS) and ethylene glycol to give 2-(bromomethyl)-2-methyl-3-oxapentane-1,5-diol (**9**) in 56% yield. Compound **9** was treated with thionyl chloride to give the corresponding dichloride (**10**) in 47% yield, followed by the reaction with NaI in acetone to afford the triiodide (**11**) in 48% yield. Compound **11** was treated with 8-hydroxyquinoline in diglyme in the presence of *t*-BuOK and 18-crown-6 at 155 °C for 4 days to give **1** as a pale yellow, viscous liquid in 44% yield. Compounds **2a**−**c** and **3** were prepared from ethylene glycol monomethallyl ether (**12a**) as the starting material, as shown in Scheme 2. Compound **12a** was bromoalkoxylated with NBS and ethylene glycol to give 4-(bromomethyl)-4-methyl-3,6-dioxaoctane-1,8-diol (**13a**). Compound **13a** was treated with thionyl chloride to give the corresponding dichloride (**14**) in 83% yield from **12a**, followed by the reaction with 8-hydroxyquinoline in ethanol in the presence of KOH at refluxing temperature for 4 days to afford **15** in 79% yield. Interestingly, under these reaction conditions, the bromo group did not react with the 8-hydroxyquinoline. Thus, ligands **2a**−**c** were prepared by the modification of **15** with the corresponding phenols according to almost the same procedure used for **1** in 67−74% yields. Concerning ligand **3**, the hydroxyl groups of **13a** were protected by the treatment with 3,4-dihydro-2*H*-pyran according to the conventional method, and then the compound was reacted with ethylene glycol mono-2-tetrahydropyranyl ether under the basic conditions, followed by the deprotection to give **18a**. The following reactions were carried out according to almost the same procedure used for **15** to give **3**. Ligand **4** was also prepared by using diethylene glycol monomethallyl ether (**12b**) as the starting material and the corresponding diethylene glycol analogue in place of the ethylene glycol derivative in the case of **3**, as shown in Scheme 2. The reference compound **5** was obtained from tris(hydroxymethyl)ethane via five steps according to a modification of the established procedures (Scheme 3). Elongation of the oxyethylene units was done by the conventional method using the reaction with monobromoacetic acid, esterification with methanol, and then the following reduction with $LiAlH_4$. The following synthetic procedure was the same as that used for **3** and **4**. All structures were ascertained by ^1H NMR and IR spectroscopy, mass spectrometry, and elemental analysis (Experimental Section).

Scheme 2



Solvent Extraction. Extraction profiles conducted under the conditions using equimolar amounts of the

Scheme 3

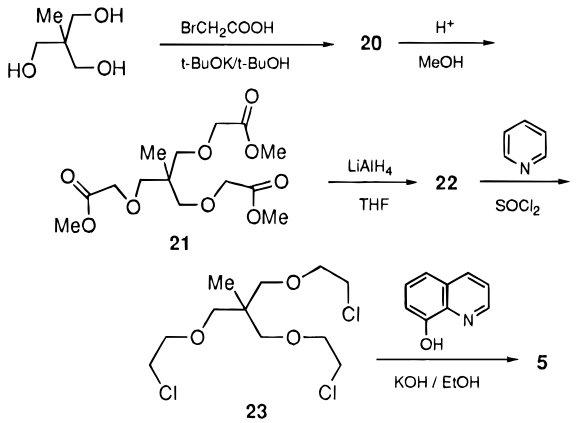


Table 1. Solvent Etraction of Alkali Metal Picrates[a]

	extractability (%)				
compd	Li^+	Na^+	K^+	Rb^+	Cs^+
1	11	67	18	9	2
2a	4	33	30	14	4
2b	3	13	19	10	5
2c	<1	4	5	3	4
3	3	11	34	13	7
4	3	23	44	36	19
5	4	7	9	4	2
6[b]	3	4	3	3	4
7[b]	4	9	36	32	18
8[c]	<1	27	11	9	2

[a] Extraction conditions: dichloromethane (10 mL)/water (10 mL); [MOH] = 5×10^{-2} M; [extractant] = [picric acid] = 5×10^{-4} M; 25 °C; 9 h. [b] Reference 4b. [c] Octyl-15-crown-5.

ionophore and alkali metal picrate[10] are shown in Table 1. First, the effect of the difference in the structure near the pivot position of the ligands on the complexation property was evaluated. Ligands **3** and **5** are structurally regarded to be derived from 2-methylglycerol and tris(hydroxymethyl)ethane, respectively. Although both ligands **3** and **5** possess the same heteroatoms (nine) and almost the same structure, their extractabilities toward alkali metal picrates are remarkably different. For example, ligand **3** showed much higher extractability toward K^+ than ligand **5** did. This result may indicate that three arms of ligand **3** cooperatively coordinate K^+; on the other hand, in the case of ligand **5**, one of the arms is not used in the complexation with the cation.

To verify the effectiveness of the 2-methylglycerol structure, the extractabilities of ligands **1**−**4** were examined. Ligand **1**, the most rigid and smallest ligand in this study, showed much higher extractability and selectivity toward Na^+ in comparison with octyl-15-crown-5 (**8**). As expected from CPK model examinations, the extractabilities toward K^+ increase in the order **1** < **2a** < **3** < **4**, which corresponds to the enlargement of cavity size by elongation of the oxyethylene chain. Although ligand **4** showed the highest extractability toward K^+, the cation selectivity was moderate. This finding shows that this strategy for the design of synthetic cation receptors is especially effective for small cations. Tripodal ligand **3** showed much higher extractability toward all alkali metal cations, especially toward K^+, than the corresponding acyclic ligand **6** having the same oxyethylene chain without an additional third arm, and the extractability of **3** toward K^+ was comparable to **7**, which showed the best extractability in the series of the oligoethylene glycol derivatives having two quinolinyloxy moieties at both ends.[4b] This result also indicates the importance of cooperative coordination of three arms for high complexing ability; therefore, the 2-methylglycerol skeleton is suggested to be necessary for arranging the three arms in one direction.

Ligand **2c** is an isomer of ligand **2b** and possesses the same heteroatoms; one of the oxygen atoms of the former is unable to participate in the coordination with the cation, and thus, the extractability of the former is inferior to that of the latter. The fact that ligands **1** and **3** showed the Na^+ and K^+ selectivity, respectively, also supports the existence of the three-dimensional coordination sphere toward alkali metal cations.

Table 2. Stability Constants in THF[a]

compd	log *K* (Na^+)	log *K* (K^+)	selectivity (Na^+/K^+)
1	4.79	3.71	12
2a	3.98	3.76	1.7
3	3.76	4.23	0.3
4	3.59	4.12	0.3
5	2.99	2.81	1.5
6	3.23	3.23	1.0
7	3.68	3.96	0.52
18-crown-6	4.49	6.26	0.017
	4.32[b]	6.10[b]	0.017
16-crown-5	3.83	3.02	6.5
	3.51[b]	2.63[b]	7.6

[a] Obtained from the calculation based on the absorption of the picrate anion in THF at 380 nm in the UV spectrum. [b] Measured by ion-selective electrode; ref 8b.

The Stability Constants. The stability constants of ligands **1**−**5** toward Na^+ and K^+ measured in THF at 25 °C[11] are summarized in Table 2 along with the data of the reference compounds. The profile of the stability constants toward Na^+ and K^+ substantively corresponded to that of solvent extraction. It is noteworthy that the stability constant (4.79) of **1** toward Na^+ was found to be about 10 times that of 16-crown-5 (3.83), whose cavity size is suitable for Na^+, and the Na^+/K^+ selectivity of ligand **1** was also better than that of 16-crown-5. As expected from the extraction data, ligands **3** and **4**, which possess a larger cavity than **1**, showed the selectivity toward K^+. The stability constant (4.23) toward K^+ of **3** was found to be 10 times that of **6** (3.23) having the same oxyethylene chain and to exceed that of **7** (3.96). This excellent complexation ability of ligand **3** toward K^+ is reasonably explained by considering the cooperation of the three electron-donating arms for the uptake of the cation. On the other hand, further elongation of the oxyethylene chain resulted in decrease of the complexing ability toward K^+. This finding shows that the fit of the cation size and the cavity size of the ligand is important for the cation recognition of this type of tripodal ligands, as often observed in the crown ether.

UV Spectrometry. Further evidence for the three-dimensional cavity was given by the UV spectroscopy study. The position of the UV spectrum of the picrate anion is a measure of the type of the ion pair.[12] When ligand **1** complexed with sodium picrate or **3** and **4** complexed with potassium picrate in THF, respectively, an absorption peak at 380 nm was observed as shown in Table 3. This absorption was assigned to the loose ion

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Table 3. UV Absorption Maximum of Picrate Anion in THF

	Na^+		K^+	
compd	[L]/[P] = 1[a]	[L]/[P] = 5	[L]/[P] = 1	[L]/[P] = 5
1	380[b]	381	361	368
2a	360	380	369	380
3	356	368	380	380
4	354	365	381	382
5	353	358	359	362
6[c]	354	358	361	367
7[c]	352	355	358	378

[a] [L] = [ligand]; [P] = [picrate anion] = 5×10^{-5} M. [b] In nm. [c] Reference 4b.

Table 4. Change in Chemical Shift[a] in ^{1}H NMR

compd	salt	H2	H3	H4	H5	H6	H7
1	NaSCN	−0.44	−0.10	0.08	0.11	0.10	−0.04
	KSCN	0.06	0.05	0.08	−0.06	0.13	−0.15
2a	NaSCN	−0.34	−0.04	0.02	−0.03	−0.03	0.04
	KSCN	−0.78	−0.37	−0.02	−0.07	0.02	0.09
3	NaSCN	−0.57	−0.42	−0.21	−0.07	−0.18	0.01
	KSCN	−0.92	−0.41	−0.09	0.10	−0.04	−0.04
4	NaSCN	−0.09	−0.02	−0.03	−0.03	0.00	−0.14
	KSCN	−0.12	0.00	−0.08	−0.10	−0.27	−0.87
5	NaSCN	−0.33	−0.07	−0.10	−0.16	−0.01	0.01
	KSCN	−0.25	−0.03	0.01	−0.08	0.03	−0.02
6[b]	NaSCN	−0.51	−0.27	−0.15	−0.03	0.02	0.11
	KSCN	−0.47	−0.13	−0.02	0.00	0.03	0.01
7[b]	NaSCN	−0.08	−0.02	−0.05	−0.03	−0.09	0.16
	KSCN	−0.05	0.09	−0.04	−0.17	−0.31	−0.73

[a] $\Delta\delta$(ppm) = δ(MSCN) − δ(none); [ligand] = [MSCN]; $CDCl_3$; 27 °C. [b] Reference 4b.

pair. On the other hand, both the combinations of **5** and sodium picrate or **6** and potassium picrate hardly showed a bathochromic shift, which indicates that they formed the contact ion pair. This large difference between the ligands possessing the 2-methylglycerol structure (**1**−**4**) and the others (**5**, **6**) should be attributable to the three-dimensional coordination of these ligands toward alkali metal cations. Furthermore, an interesting result was observed in the case of ligand **7**. Although ligand **7** showed nearly the same extractability toward K^+ as **3** and **4**, the combination of **7** and potassium picrate hardly showed a bathochromic shift when an equimolar of potassium picrate was added. By considering the fact that the combination of **3**, of which the oxyethylene chain is shorter than that of **7**, and potassium picrate showed a large bathochromic shift when an equimolar of potassium picrate was mixed, this result strongly supports the existence of the three-dimensional coordination by using the three arms simultaneously. The UV absorption of a 5-fold concentration of sodium picrate (or potassium picrate) and compound **2a** in THF was also observed at 380 nm.

Chemical Shift in ^{1}H NMR. To evaluate the detailed conformations of the ligands in solution, changes in the chemical shifts of the quinoline group upon the addition of NaSCN or KSCN in $CDCl_3$ were measured with ^{1}H NMR. When a donor atom participates in coordination with a metal ion, chemical shifts of the neighboring protons generally tend to move downfield. On the contrary, the paramagnetic effect of the aryl groups may produce an upfield shift. The results are shown in Table 4.[13]

An interesting trend was observed in chemical shifts of the ^{1}H NMR spectra upon complexation with alkali metal thiocyanates, which is regarded as a measure of the extent of the proximity of the quinoline rings.[3,4] Ligand **1**, which displayed a favorable selectivity for Na^+, showed a fairly large upfield shift in H_2 and H_3 of quinoline when NaSCN was added. As expected by the CPK model examination, this result clearly shows the proximity of the three quinoline rings based on the formation of the three-dimensional coordination sphere toward Na^+ like that of cryptand.[3,4] Both ligands **3** and **4** showed K^+/Na^+ selectivity by the measurement of the stability constant and the extractability; however, a difference in the pattern of the change in chemical shifts was observed when KSCN was added. The upfield of H_2 and H_3 in ligand **3**, upon the addition of KSCN, indicates that the conformation of the complex was considered to resemble that of **1**. On the other hand, ligand **4** showed the upfield of H_6 and H_7 upon the addition of KSCN, which was also observed in the case of **7**. This behavior was reasonably explained by considering that only two of the oxyethylene chains of **4** surround K^+ with a pseudo-ring conformation, similar to the way of an 18-crown-6 as previously reported in the complexation of ligand **7**.[3,4] We speculate that the number of donor atoms is so large that the three arms cannot coordinate toward K^+ simultaneously. In this case, π-stacking of two of the three quinoline rings mainly contributes to the stabilization of the complex with the K^+. Therefore, the complexing ability of ligand **4** probably resembled that of **7**.

Table 5. Competitive Passive Transport Data[a] toward Li^+, Na^+, and K^+

				selectivity		
compd	Li^+	Na^+	K^+	Na^+/Li^+	Na^+/K^+	K^+/Na^+
1	0.83	43	1.5	52	29	
3	0.088	0.57	9.8	6.5		17
4	0.27	1.9	28	7.0		15
6	0.46	1.0	1.7	2.2		1.7
7	0.32	1.7	4.0	5.3		2.4
8[b]	0.34	1.6	3.2	4.4		2.0

[a] $\times 10^7$ mol/h. Transport conditions: aqueous phase 1 (10 mL), [LiCl] = [NaSCN] = [KSCN] = $[Me_4NOH]$ = 0.1 M; organic phase (CH_2Cl_2, 20 mL), [carrier] = 2.5 mM; aqueous phase 2 (10 mL); 25 °C. [b] Octyl-15-crown-5.

Bulk Liquid Membrane Transport. Membrane transport is an important method for estimating the complexation properties for metal cations. Selective separation of alkali metal cations was carried out by the liquid membrane transport method. The competitive passive transport conditions and the results in the presence of Li^+, Na^+, and K^+ are summarized in Table 5. Ligand **1** showed an excellent transport ability and selectivity toward Na^+ among Li^+, Na^+, and K^+, as expected from the extractabilities, although octyl 15-crown-5 hardly transported any metal cations under these transport conditions. Elongation of the oxyethylene chain of the ionophores changed the cation selectivity from Na^+ to K^+. Ligands **3** and **4** selectively transported K^+, and the latter had higher transport ability than the former for all cations used in this transport experiment. Interestingly, ligands **6** and **7** scarcely transported cations as shown in Table 5. This result indicates that higher lipophilicity of the complexes of tripodal ligands due to the three-dimensional coordination and the high complexation abilities themselves accelerated the transport.

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Conclusions

In this paper, we described the design, synthesis, and properties of two types of tripodal ligands, which differ in the basic skeleton. Strong complexation properties for alkali metal cations were attained by selecting the 2-methylglycerol unit (**1**−**4**), not the tris(hydroxymethyl)-ethane unit (**5**), as the basic skeleton in the design of C-pivot tripodal ligands. The methyl group substituted on the pivot carbon may contribute to the arrangement of the three electron-donating arms into the required conformation around the cavity. As a result, among the ligands examined in this study, **1** was found to possess an excellent affinity toward Na^+ in comparison with 15-crown-5 and 16-crown-5 ethers. This strategy for the molecular design of C-pivot tripodal ligands is potentially useful for the development of novel types of host compounds for metal cations.

Experimental Section

^{1}H NMR spectra were taken at 400 MHz using tetramethylsilane as the internal standard. Ethylene glycol monomethallyl ether (**12a**) and diethylene glycol monomethallyl ether (**12b**) were prepared according to the literature.[8]

2-(Bromomethyl)-2-methyl-3-oxapentane-1,5-diol (9). To a stirred suspension of *N*-bromosuccinimide (NBS) (53.4 g, 0.30 mol) in ethylene glycol (186.21 g, 3.0 mol) was added β-methallyl alcohol (21.63 g, 0.30 mmol) cooled in an ice bath over a period of 1 h. The resulting mixture was further stirred at room temperature for another 6 h. Then, 300 mL of aq Na_2CO_3 (10%) was added, and the mixture was extracted with dichloromethane (300 mL × 3). After evaporation, the residue was purified by chromatography over silica gel (acetone/hexane = 1/1) to give **9** as a colorless liquid (7.50 g, 56%): ^{1}H NMR ($CDCl_3$) δ 1.30 (s, 3H), 3.40 (s, 2H), 3.44−3.75 (m, 8H); IR (neat) 3500−3250, 2950, 1400, 1300, 1200, 1080, 970, 900 cm^{-1}; MS (CI) (*m*/*z*) 213 ($M^+ + 1$, 100), 195 (55), 133 (20), 63 (55).

2-(Bromomethyl)-1,5-dichloro-2-methyl-3-oxapentane (10). After **9** (10.65 g, 50 mmol) and pyridine (5 mL) were dissolved in chloroform (50 mL), thionyl chloride (23.79 g, 0.20 mol) was added dropwise to the mixture over a period of 1 h. The resulting mixture was further stirred at reflux temperature for another 48 h. After the mixture was cooled to room temperature, aq Na_2CO_3 (10%, 200 mL) was added, and the mixture was extracted with dichloromethane (200 mL × 3). After evaporation, the residue was purified by chromatography over silica gel (acetone/hexane = 1/19) to give **10** as a slightly yellow liquid (5.90 g, 47%): ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 3H), 3.45−3.74 (m, 8H); IR (neat) 2950, 1460, 1370, 1300, 1200, 1100, 1040, 960, 720, 650 cm^{-1}; MS (CI) (*m*/*z*) 251 ($M^+ + 1$, 100), 171 (65).

1,5-Diiodo-2-(iodomethyl)-2-methyl-3-oxapentane (11). After **10** (2.00 g, 8 mmol) and NaI (17.99 g, 0.12 mol) were dissolved in acetone (100 mL), the resulting mixture was stirred at reflux temperature for 72 h. After being cooled to room temperature, the mixture was filtered and evaporated in vacuo. Water (100 mL) was added to the residue, and the mixture was extracted with dichloromethane (100 mL × 3). After evaporation, the residue was purified by chromatography over silica gel (acetone/hexane = 1/9) to give **11** as a yellow liquid (1.84 g, 48%): ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 3H), 3.23−3.72 (m, 8H); IR (neat) 2950, 1420, 1380, 1260, 1100, 720, 650 cm^{-1}; MS (EI) (*m*/*z*) 339 (100), 155 (100).

2-Methyl-2-[(8-quinolinyloxy)methyl]-1,5-bis[8-(quinolinyloxy)]-3-oxapentane (1). To a stirred suspension of 8-hydroxyquinoline (2.45 g, 17 mmol), potassium *tert*-butyl oxide (1.26 g, 11.2 mmol), and 18-crown-6 (24 mg, 9.35×10^{-2} mmol) in diglyme (20 mL) was added **11** (0.90 g, 1.87 mmol). The resulting mixture was stirred at 155 °C for 48 h. After the mixture was cooled to room temperature, dichloromethane (100 mL) was added, and the insoluble matter was removed by filtration. Water (100 mL) was added, and the mixture was extracted with dichloromethane (100 mL × 3). After evaporation, lower boiling point distillates were removed under reduced pressure (120 °C/0.05 Torr) and the residue was purified by chromatography over alumina (acetone/dichloromethane = 1/19) to give **1** a slightly yellow, viscous liquid (0.44 g, 44%): ^{1}H NMR ($CDCl_3$) δ 1.75 (s, 3H), 4.29−4.66 (m, 8H), 7.20 (dd, 3H, J = 8.3, 2.0 Hz), 7.31 (dd, 3H, J = 8.3, 2.0 Hz), 7.37 (dd, 3H, J = 8.3, 4.4 Hz), 7.42 (t, 3H, J = 8.3 Hz), 8.06 (dd, 3H, J = 8.3, 1.7 Hz), 8.87 (dd, 3H, J = 4.4, 1.7 Hz); IR (neat) 2900, 1500, 1380, 1320, 1280, 1120, 820, 800, 760, 740 cm^{-1}; MS (EI) (*m*/*z*) 531 (M^+, tr), 198 (100). Anal. Calcd for $C_{33}H_{29}O_4N_3 \cdot H_2O$: C, 72.12; H, 5.68; N, 7.64. Found: C, 71.72; H, 5.88; N, 7.99.

4-(Bromomethyl)-4-methyl-3,6-dioxaoctane-1,8-diol (13a). The synthetic procedure was almost the same as that used for **9**. To a stirred suspension of NBS (53.40 g, 0.30 mol) in ethylene glycol (186.21 g, 3.0 mol) was added ethylene glycol mono-β-methallyl ether (**12a**) (34.80 g, 0.30 mmol) dropwise over a period of 30 min under cooling in an ice bath. The resulting mixture was further stirred at 50 °C for another 20 h. After the mixture was cooled to room temperature, aq Na_2CO_3 (10%, 200 mL) was added, and the mixture was extracted with dichloromethane (200 mL × 4). The crude intermediate (16.63 g) was used for the next step without further purification.

8-(Bromomethyl)-8-methyl-3,6,9,12-tetraoxatetradecane-1,14-diol (13b). The synthetic procedure was almost the same as that used for **9**. The crude intermediate was used for the next step without further purification.

4-(Bromomethyl)-1,8-dichloro-4-methyl-3,6-dioxaoctane (14). The synthetic procedure was almost the same as that used for **10**. The crude compound was purified by chromatography over silica gel (acetone/hexane = 1/19) to give **14** as a slightly yellow liquid (7.55 g, 83% based on **12a**): ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 3H), 3.48−3.77 (m, 12H); IR (neat) 2950, 1420, 1300, 1200, 1120, 980, 760 cm^{-1}; MS (CI) (*m*/*z*) 295 ($M^+ + 1$, 20), 215 (100).

8,8′-[[1-(Bromomethyl)-1-methyl-1,2-ethanediyl]bis[(oxy-2,1-ethanediyl)oxy]]bisquinoline (15). 8-Hydroxyquinoline (10.89 g, 75 mmol) and KOH (4.95 g, 75 mmol) were dissolved in ethanol (150 mL). The mixture was refluxed for 2 h, and then the solution of **14** (7.32 g, 24 mmol) in ethanol (20 mL) was added dropwise over a period of 2 h. The mixture was stirred for another 4 days. After being cooled to room temperature, the mixture was filtered and evaporated. Water (200 mL) was added, and the mixture was extracted with dichloromethane (200 mL × 5). After evaporation, the residue was purified by chromatography over alumina (dioxane/benzene = 1/9−3/7) to give **15** as a slightly yellowish, viscous liquid (10.06 g, 79%): ^{1}H NMR ($CDCl_3$) δ 1.31 (s, 3H), 3.50−4.40 (m, 12H), 7.10−7.12 (m, 2H), 7.36−7.44 (m, 6H), 8.09−8.11 (m, 2H), 8.92−8.93 (m, 2H); IR (neat) 2900, 1600, 1500, 1100, 880, 760 cm^{-1}; MS (EI) (*m*/*z*) 513 ($M^+ + 1$, 100), 172 (100). Anal. Calcd for $C_{26}H_{27}O_4N_2Br \cdot H_2O$: C, 58.99; H, 5.52; N, 5.29. Found: C, 59.37; H, 5.35; N, 5.15.

8,8′-[[1-Methyl-1-[(8-quinolinyloxy)methyl]-1,2-ethanediyl]bis[(oxy-2,1-ethanediyl)oxy]]bisquinoline (2a). The synthetic procedure was almost the same as that used for **1**. To a stirred suspension of 8-hydroxyquinoline (5.80 g, 40 mmol) and potassium *tert*-butyl oxide (2.24 g, 20 mmol) in diglyme (20 mL) was added **15** (1.02 g, 2.0 mmol). The resulting mixture was stirred at 150 °C for 48 h. After the mixture was cooled to room temperature, dichloromethane (100 mL) was added to the residue and the insoluble matter was removed by filtration. Water (100 mL) was added to the solution, and the mixture was extracted with dichloromethane (100 mL × 4). After evaporation, the lower-boiling point matter was removed under reduced pressure (100 °C/0.1 Torr) and then the residue was purified by chromatography over alumina (acetone/dichloromethane = 1/19) to give **2a** as a slightly yellow, viscous liquid (0.85 g, 74%): ^{1}H NMR ($CDCl_3$) δ 1.48 (s, 3H), 3.71−4.41 (m, 12H), 7.03 (dd, 3H, J = 8.2, 2.0 Hz), 7.31 (dd, 3H, J = 8.3, 2.0 Hz), 7.35 (dd, 3H, J = 8.3, 4.4 Hz), 7.37 (dd, 3H, J = 8.3, 8.2 Hz), 8.07 (dd, 3H, J = 8.3, 2.4 Hz), 8.89 (dd, 3H, J = 4.4, 2.4 Hz); IR (neat) 2850, 1600, 1500, 1100, 880, 760 cm^{-1}; MS (FAB-MS) (*m*/*z*) 576 ($M^+ + 1$, 100).

Anal. Calcd for $C_{35}H_{33}O_5N_3 \cdot H_2O$: C, 70.81; H, 5.94; N, 7.08. Found: C, 70.95; H, 6.04; N, 6.69.

8,8′-[[1-[(2-Methoxyphenoxy)methyl]-1-methyl-1,2-ethanediyl]bis[(oxy-2,1-ethanediyl)oxy]]bisquinoline (2b). The synthetic procedure was almost the same as that used for **2a**. The crude compound was purified by chromatography over alumina (acetone/dichloromethane = 1/49−1/19) to give **2b** as a slightly yellow, viscous liquid (0.74 g, 67%): ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 3.75−4.39 (m, 15H), 6.80−6.87 (m, 4H), 7.06−7.10 (m, 2H), 7.34−7.39 (m, 6H), 8.06−8.10 (m, 2H), 8.89−8.93 (m, 2H); IR (neat) 2950, 1600, 1580, 1500, 1460, 1380, 1320, 1260, 1100, 830, 800, 760 cm^{-1}; MS (FAB-MS) (*m*/*z*) 555 ($M^+ + 1$, 100). Anal. Calcd for $C_{33}H_{34}O_6N_2 \cdot 0.5H_2O$: C, 70.32; H, 6.26; N, 4.97. Found: C, 70.55; H, 6.30; N, 4.70.

8,8′-[[1-[(4-Methoxyphenoxy)methyl]-1-methyl-1,2-ethanediyl]bis[(oxy-2,1-ethanediyl)oxy]]bisquinoline (2c). The synthetic procedure was almost the same as that used for **2a**. The crude compound was purified by chromatography over alumina (acetone/dichloromethane = 1/199−3/97) to give **2b** as a slightly yellow, viscous liquid (0.78 g, 71%): ^{1}H NMR ($CDCl_3$) δ 1.32 (s, 3H), 3.69−4.39 (m, 15H), 6.72−6.80 (m, 4H), 7.04−7.10 (m, 2H), 7.33−7.40 (m, 6H), 8.06−8.10 (m, 2H), 8.89−8.91 (m, 2H); IR (neat) 2950, 1600, 1580, 1520, 1480, 1390, 1330, 1260, 1120, 840, 800, 760 cm^{-1}; MS (FAB-MS) (*m*/*z*) 555 ($M^+ + 1$, 100). Anal. Calcd for $C_{33}H_{34}O_6N_2 \cdot 0.5H_2O$: C, 70.32; H, 6.26; N, 4.97. Found: C, 70.56; H, 6.28; N, 4.80.

8,8′,8″-[(2-Methyl-1,2,3-propanetriyl)tris[(oxy-2,1-ethanediyl)oxy]]trisquinoline (3). The synthetic procedure was almost the same as that used for **15**. The crude compound was purified by chromatography over alumina (methanol/dichloromethane = 1/199) to give **3** as a slightly yellow, viscous liquid (1.45 g, 69%): ^{1}H NMR ($CDCl_3$) δ 1.21 (s, 3H), 3.55−4.35 (m, 16H), 7.06 (dd, 3H, J = 7.8, 1.5 Hz), 7.33 (dd, 3H, J = 8.3, 1.5 Hz), 7.36 (dd, 3H, J = 8.3, 4.2 Hz), 7.38 (dd, 3H, J = 8.3, 7.8 Hz), 8.06 (dd, 3H, J = 8.3, 2.0 Hz), 8.88 (dd, 3H, J = 4.2, 2.0 Hz); IR (neat) 2900, 1560, 1460, 1360, 1300, 1250, 1100, 900, 820, 780, 720 cm^{-1}; MS (CI) (*m*/*z*) 620 ($M^+ + 1$, 100), 475 (15), 172 (20), 146 (32). Anal. Calcd for $C_{37}H_{37}O_6N_3 \cdot H_2O$: C, 69.68; H, 6.16; N, 6.59. Found: C, 69.71; H, 6.46; N, 6.25.

8,8′,8″-[(2-Methyl-1,2,3-propanetriyl)tris[(oxy-2,1-ethanediyloxy-2,1-ethanediyl)oxy]]trisquinoline (4). The synthetic procedure was almost the same as that used for **15**. The crude compound was purified by chromatography over alumina (acetone/dichloromethane = 1/19) to give **4** as a slightly yellow, viscous liquid (0.96 g, 29%): ^{1}H NMR ($CDCl_3$) δ 1.25 (s, 3H), 3.40−4.40 (m, 28H), 7.10 (dd, 3H, J = 7.8, 1.5 Hz), 7.35 (dd, 3H, J = 8.2, 1.5 Hz), 7.39 (dd, 3H, J = 8.3, 4.4 Hz), 7.42 (dd, 3H, J = 8.2, 7.8 Hz), 8.11 (dd, 3H, J = 8.3, 1.7 Hz), 8.93 (dd, 3H, J = 4.4, 1.7 Hz); IR (neat) 2900, 1500, 1380, 1280, 1120, 820, 800, 760, 740 cm^{-1}; MS (EI) (*m*/*z*) 751 (M^+, tr), 607 (15), 505 (65), 172 (100), 145 (30). Anal. Calcd for $C_{43}H_{49}O_9N_3 \cdot 2H_2O$: C, 65.55; H, 6.78; N, 5.33. Found: C, 65.43; H, 6.54; N, 4.97.

1,1,1-Tris[[2-[(8-quinolinyl)oxy]ethoxy]methyl]-ethane (5). The synthetic procedure was almost the same as that used for **15**. The crude compound was purified by chromatography over alumina (dichloromethane/acetone = 3/197−3/97) to give **5** as a slightly yellow, viscous liquid (0.56 g, 55%): ^{1}H NMR ($CDCl_3$) δ 0.91 (s, 3H), 3.38 (s, 6H), 3.85−3.87 (t, 6H), 4.31−4.33 (t, 6H) 7.08 (dd, 3H, J = 8.3, 1.5 Hz), 7.34 (dd, 3H, J = 8.0, 1.5 Hz), 7.37 (dd, 3H, J = 8.1, 3.9 Hz), 7.39 (dd, 3H, J = 8.3, 8.0 Hz), 8.07 (dd, 3H, J = 8.1, 1.5 Hz), 8.91 (dd, 3H, J = 3.9, 1.5 Hz); IR (neat) 2950, 1580, 1380, 1330, 1280, 1120, 830, 800, 740 cm^{-1}; MS (CI) (*m*/*z*) 634 ($M^+ + 1$, 100), 489 (20), 146 (20). Anal. Calcd for $C_{38}H_{39}O_6N_3 \cdot H_2O$: C, 70.03; H, 6.34; N, 6.44. Found: C, 70.06; H, 6.21; N, 6.34.

Extraction Procedure. A mixture of an aqueous solution (10 mL) of alkali metal hydroxide (5×10^{-2} M) and picric acid (5×10^{-4} M) with a dichloromethane solution (10 mL) of an appropriate extractant (5×10^{-4} M) was shaken at 25 °C for 9 h. The extractability was obtained from the calculation based on the absorption of the picrate anion in the aqueous phase at 354 nm in the UV spectrum.

Measurement of Stability Constants. All of the stability constants reported herein were determined for sodium picrate or potassium picrate in THF at 25 °C, and the absorption of the picrate anion in THF at 380 nm in the UV spectrum was used for calculating the stability constants. Typically, the concentration of the guest compound was fixed to be 5×10^{-5} M in THF, and the molar ratios of host to guest were changed in the ranges from 0 to 10 by changing the concentrations of the host compound. Eight data were collected for each host−guest system, and the stability constant (K) was calculated using an iterative nonlinear least-squares curve-fitting program. In this case, 1:1 complexation was postulated.

Liquid Membrane Transport. Transport experiments were carried out in a U-shaped cell at 25 °C as described in the literature.[14] The details of the transport conditions are summarized in the footnotes of Table 5. The receiving phase was sampled from four different cells after 12, 24, 36, and 48 h and analyzed for cation concentration using a Nippon Jarrel-Ash AA-8500 atomic absorption spectrometer. The value reported in the Table 5 was the mean of four samples, and the deviations from the mean were less than 10%.

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Supporting Information Available: Preparation and characterization for compounds **16**−**23** (4 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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